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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,822	10/16/2003	Manisha Sharadchandra Deshpande	RELIA.P-113	8483

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EXAMINER

AFREMOVA, VERA

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 04/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/686,822	Applicant(s) DESHPANDE ET AL.	
	Examiner Vera Afremova	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 1,2,5,15 and 17-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3,4,6-14,16,22 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II (claims 3, 4, 6-14, 16, 22 and 23) in the reply filed on 1/23/2006 is acknowledged.

The traversal is on the ground(s) that there is no serious burden in searching and examining all groups of claims. This is not found persuasive because different groups of claims are drawn to distinct products comprising different materials as claimed and, thus, the references that would be applied to one group of claims would not necessarily anticipate or render obvious the other group(s). Moreover, as to the question of burden of search, the literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exists. Clearly different searches and issues are involved with each group. For these reasons, the restriction requirement is deemed proper and is adhered to. The restriction requirement is hereby made FINAL.

Claims 1, 2, 5, 15 and 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected groups of inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 1/23/2006.

Claims 3, 4, 6-14, 16, 22 and 23 are under examination in the instant office action.

With respect to the election of species, applicants clearly recognize that there are five (5) patentably distinct species in the original claims (see last responses page 9, par. 6) and that these distinct species are 1) dermal fibroblasts; 2) adipose stromal cells; 3) osteogenic cells derived from adipose stromal cells; 4) chondrocytes; 5) osteoblasts as originally claimed. For example: see original claims 3 and 9.

In response to the election of species requirement applicants elected to prosecute “fibroblasts and cells of mesenchymal origin” (last response page 9, par. 2). In view of applicants’ definitions in the specification (page 6, lines 9-10) the presently elected “fibroblasts and cells of mesenchymal origin” are “fibroblastic cells of mesenchymal origins” such as “dermal equivalent made from dermal fibroblasts” and, thus, “dermal fibroblast”. Applicants clearly confirm that “fibroblasts” are the elected species (last response page 9, par. 6). The other originally listed species including adipose stromal cells, osteogenic cells derived from adipose stromal cells, chondrocytes and osteoblasts are not the fibroblasts. Although adipose stromal cells, osteogenic cells derived from adipose stromal cells, chondrocytes might be considered as cells of mesenchymal origin and/or they might derive from mesenchymal stem cells, these claimed cells are outside of the elected species “fibroblasts”. The term “cells of mesenchymal origin” is generic.

Thus, in the instant office action the claimed invention is examined as being drawn to the use of the elected species such as “fibroblast” or “dermal fibroblasts” as pointed out by applicants (response page 9) and as supported by the applicants’ generic and particular disclosure (specification page 6, lines 9-10; specification page 18, line 16; specification page 20, table 1).

Claim Rejections - 35 USC § 112

New matter

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Insertion of the limitation “mesenchymal cells” has no support in the as-filed specification. The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited species that would show possession of the concept of the use of “mesenchymal cells”.

The as-filed specification is lacking particular definitions with respect to the meaning of the newly inserted term “mesenchymal cells”.

The as-filed specification uses the term “mesenchymal stem cells” as related to the prior art only (specification page 4, par. 3). The as-filed specification uses the term “cells of mesenchymal origin” as related to the fully differentiated dermal fibroblasts, adipose stromal cells, osteogenic cells derived from adipose stromal cells and chondrocytes as related to the object of the present invention (page 6, par. 3).

The particular disclosure describes the use of fully differentiated dermal fibroblasts, adipose stromal cells, chondrocytes and osteoblasts only (page 18). The particular disclosure does not describe the use “mesenchymal stem cells”.

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Thus, given broadest reasonable interpretation and as based on particular disclosure there is no support in the as-filed specification for the newly limited species of “mesenchymal cells”.

This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of limitation “mesenchymal cells” is considered to be the insertion of new matter for the above reasons.

Indefinite

Claims 3, 4, 6-14, 16, 22 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite because it is unclear what are the final properties of the claimed “tissue-like organizations of cells”. The specific definitions are lacking in the specifications and the “tissue-like organizations of cells” are broadly described by applicants as “living, cellular, tissue substitutes” (page 13, last par.). The presently claimed invention appears to be presented in a form of product-by-process. However, manipulation steps are not clearly pointed out. It is unclear what final properties would result from the manipulations steps as intended. The claimed phrase “not necessarily limited to these cell types” and the claimed phrase “can be made to assume different forms” do not identify any specific characteristics. The metes and bounds of the claim cannot be determined.

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Claim 3 depends on non-elected claim 1 and, thus, it is uncertain what limitations of claim 1 would be “according” and/or “including”. It is unclear what final properties would result from the manipulations steps as intended.

Claims 3, 4, 22 and 23 are indefinite with respect to term “macroscopic” in the lack of applicants’ definitions. The final size or volume or amount of the claimed product is uncertain as claimed and when read in the light of specification.

Claim 9 is indefinite with respect to the newly inserted term “mesenchymal cells” in the lack of specific applicants’ definitions. This term is interpreted as having generic meaning relating to “fibroblast cells of mesenchymal origin” such as “dermal fibroblasts” in particular.

Claims 10-13 are indefinite with respect to term “macromass culture” in the lack of applicants’ definitions. In the instant office action this term is interpreted as drawn to the use of “high cell seeding densities” for engineering the product-made-by-process.

Claims 13 and 14 are indefinite with respect to the claimed term “flexibility” and its relationship with the final properties of the claimed product.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 4, 6-14, 16, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,755,814 (Berg et al.).

Claims are directed to a tissue-like preparation of cells suitable for implantation and/or for in vitro drug testing wherein the tissue-like preparation of cells is 3-dimensional, free of scaffold and/or artificial matrices and made from dermal fibroblasts. The claimed tissue-like preparation of cells are not limited by any specific form, the claimed tissue-like preparation of cells do not requires complex media for culturing and they are obtained in culture vessels.

US 5,755,814 (Berg et al.) discloses dermal fibroblast preparation grown in culture vessels in basic DMEM with serum and in the absence matrices (col. 9, lines 38-46). The cited patent teaches that fibroblasts attached to plastic dishes and proliferated better without matrices than fibroblasts in the presence of matrices. The dermal fibroblast preparation grown as attached layer on plastic dishes without matrices is the same cell preparation as the presently claimed "tissue-like organization of cells" within the meaning of the claims and in the light of specification. The cited fibroblasts are made dermal fibroblasts, they not have scaffolds, they are 3-dimentional in "nature" (claim 4), they are "generated wholly using cells alone and culture medium" (claim 6) without supplements (claim 7) or serum-free medium requirement (claims 12). The cited patent teaches that amounts of cells in final preparation depends on cells density (see fig 3 as related to "plastic" culture free of scaffold or artificial matrices) and, thus, "cell seeding densities ... favors tissues formation" within the meaning of the claims (claim 10). The cited dermal fibroblast cell preparation is not limited by any specific form, does not require the complex media for culturing and obtained in culture vessels as the presently claimed fibroblast cell preparations. The cited dermal fibroblast cell preparation comprises living cells and, thus, can be used for as tissue substitute for implantation and/or for in vitro drug testing within the meaning of the claims. Thus, the cited document anticipates the claimed invention.

Claims 3, 4, 6-14, 16, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Furukawa et al. ("Formation of human fibroblast aggregates (spheroids) by rotational culture". Cell Transplantation. 2001, Vol. 10, pages 441-445).

Claims as above.

The reference by Furukawa et al. discloses preparation of 3-dimensional fibroblast aggregates obtained by seeding cells at "high density", and, thus, "macromass culture" within the meaning of the claims. The reference describes that 5 ml suspension 1.66×10^6 cells/ml are inoculated into dish with diameter 35 mm and, thus the seeding density is as follows: $5 \times 1.66 \times 10^6 / 5.4 \text{ cm}^2 = 1.5 \times 10^6 \text{ cells/cm}^2$ wherein $\pi r^2 = 3.14 \times (3.5 \text{ cm} / 2)^2 = 5.4 \text{ cm}^2$. The claimed invention encompasses the use of "high density" seeding of about 10^6 cells/cm^2 as it is used for generating fibroblast aggregates of the cited reference.

Although the cited reference describes that fibroblast cells are grown with shaking or by rotating culture, the final product is 3-dimensional tissue-like organizations of cells as the claimed product. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. MPEP 2113. Although the cited reference describes that fibroblast cells are grown on medium with supplements including insulin, dexamethasone, etc. the claimed invention does not exclude the supplements described in the cited reference. Moreover, the final components of the claimed cellular product are not defined by the claimed invention. Thus, the 3-dimensional tissue-like dermal fibroblast aggregates disclosed by Furukawa et al. are identical to the claimed tissue-like organization of cells made from dermal fibroblasts. Therefore, the cited document anticipates the claimed invention.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

April 12, 2006

A handwritten signature in black ink, appearing to read 'V. Afremova', with a long horizontal flourish extending to the right.

VERA AFREMOVA

PRIMARY EXAMINER